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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/077,392	02/15/2002	Kathryn F. Sykes	UTSD:557USD2	4223

7590 06/03/2004

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EXAMINER	
AKHAVAN, RAMIN	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 06/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/077,392	SYKES ET AL.	
	Examiner	Art Unit	
	Ramin (Ray) Akhavan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *54-62,97-104 and 106-109* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *54-58,97-101,104 and 106-109* is/are allowed.

6)☒ Claim(s) *59-61* is/are rejected.

7)☒ Claim(s) *62, 102 and 103* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of an amendment, filed 03/22/2004, in which claims were amended (claims 54-55, 57, 59-62, 102 and 108). Claims 54-62, 97-104 and 106-109 are pending in the instant application. Any grounds of rejection or objection not repeated herein are withdrawn.

Claim Objections

Applicant is advised that since claims 55 and 97 are allowable, claims 102 and 103 are objected to under 37 CFR 1.75 as being a substantial duplicate thereof, respectively. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). In each case it appears the same subject matter is being claimed in claims 102 and 103 as previously claimed in claims 55 and 97, i.e. obtaining an ORF (or DNA segment) through PCR or chemical synthesis. Appropriate correction is required.

Claims 60-62 are objected to as being improperly dependent upon a subsequent claim. A claim can only be dependent from a prior claim. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. **Claims 59-61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.**

Claim 59 depends from itself. Therefore the claim is vague and indefinite.

With respect to claims 60-61, the claims recite the term "defined as" which is vague and indefinite. Furthermore claim 60 is drawn to a method of producing antibodies, while it ultimately depends from base claim 54, which is directed to a method of "screening a biological response". Similarly, claim 61 is directed to a method of "immunizing the animal", which can be interpreted to mean providing protective immunity, while base claim 54 is directed to a screening assay. Given that the base claim and dependant claims in each case are drawn to two distinct processes, it is unclear how "defined as" should be interpreted to delineate the claims' metes and bounds. For example, does the change from an method of assay to a method of antibody production or immunization include additional steps?

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. **Claim 61 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.**

The claim is directed to a method of "immunizing [an] animal". The term "immunizing" (or vaccination) confers the meaning that the process results in protective immunity for the animal against a pathogen. However, the disclosure is not enabling for immunizing or providing protective immunity to an animal.

The test for enablement is whether one skilled in the art could make use the claimed invention from the disclosure in the specification coupled with information known in the art without undue experimentation. *United States v Telectronics Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988). Whether undue experimentation is required is not based upon a single factor but instead is a conclusion reached by weighing many factors which are outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). The factors include the following:

Scope/Breadth of the claims. The claim is drawn to immunization of any animal against a pathogen or subset (e.g. a single ORF) from a pathogen, using a process of providing linear or circular expression elements to the animal. It should be noted that the claims literally read as obtaining "a" linear or circular expression element, without intervening cloning or amplification. As such the biological response is in response to "a" linear or circular expression element.

Nature of the invention. The invention is drawn to a method of providing protective immunity to an animal, where the animal is subject to at least a single expression element. The expression element encodes a single ORF, which is expressed in an animal, thus eliciting an immune response that results in protective immunity ("immunization") against the pathogen.

Unpredictability of and State of the art. The art of immunization (vaccination) with nucleic acids can be quite unpredictable if not problematic. To elicit vaccination, the immune response to a particular antigen must of a certain caliber so as to protect the animal from challenge by the particular pathogen from which the antigen being expressed is derived. Notably, since the expression elements in the instant invention are not being propagated or otherwise amplified, each particular ORF or antigen would only be expressed to a limited degree, which would not necessary confer immunity. Thus, while the method may be predictable with respect to assaying for an immune response (e.g. through ELISA for antibody production), it would be unpredictable with respect to actually providing protective immunity to an animal or human.

Moreover, if an animal were subjected to a large dose of a plurality of expression elements, there would be unpredictability with respect to adverse side effects (e.g. toxic shock) or even the potential for integration of the naked DNA into the host genome, resulting in a multitude of unexpected outcomes. For example, if the foreign DNA integrates near a protooncogene or a tumor suppressor, the integration could activate the former or inactivate the latter. (e.g. *Lai et al. DNA Vaccines. Crit. Rev. Immun. 1998; 18:449-484, at p. 451, col. 1, ¶ 1*). More particularly with Expression Library Immunization (ELI), the process must be performed in small animals in order to expose the critical immunogenic proteins of infectious agents; "A limitation [for ELI] includes the difference between mice and man in response to known antigens, for example matrix A protein for CTL responses to influenza virus; that epitope is limited to HLA-A2 in humans and is lacking in mice." (*Id. at p. 452 bridging to 453*). Thus even if successful immunity were achieved in an animal model, such as mice or rat, this would not

necessarily mean that the invention could be used in larger animals or humans without a great deal more experimentation.

Amount of guidance provided. There is guidance provided with respect to ELI in a rodent model to screen for biological response. However, there does not appear to be any guidance provided with respect to larger animals. Moreover, the bulk of the guidance provided is directed to making the expression elements and assaying expression levels in cell culture or in mice. There does not appear to be any guidance present particular to the problems of producing protective immunity or immunizing an animal.

Number of working examples. There do not appear to be any working examples that actually show protective immunity, where an animal is challenged with a particular pathogen to show that there is a *protective* immune response.

Amount of Experimentation Required. The level of skill in the art required to practice the claimed invention is high. Given the unsolved hurdles to successful practicing of the invention, the level of unpredictability in the art and lack of working examples, it must be considered that the skilled artisan would be required to conduct trial and error experimentation of an undue nature in order to attempt to practice the claimed invention.

Conclusion

Claims 59-61 are rejected. Claim 62 would be allowable, save its improper dependency from a subsequent claim. Claims 54-58, 97-104 and 106-109 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ramin (Ray) Akhavan whose telephone number is 571-272-0766.

The examiner can normally be reached on Monday- Friday from 8:00-4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

GERRY LEFFERS
PRIMARY EXAMINER